04-090 JC04 Rec'd PCT/PTO 06 APR 2001

FORM PTO-1390 (Modified) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE
REV 5-93

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR
29988/AX98115	09/807146

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP99/07518	7 October 1999	9 October 1998

TITLE OF INVENTION

POLYGLUCAN AND POLYGLUCAN DERIVATIVES WHICH CAN BE OBTAINED FROM AMYLOSUCRASE BY BIOCATALYTIC PRODUCTION IN THE PRESENCE OF BIOGENIC SUBSTANCES

APPLICANT(S) FOR DO/EO/US

Karl-Christian GALLERT, Holger BENGS, and Claus SIMANDI

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ A copy of the International Search Report (PCT/ISA/210).
8. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 20 below concern document(s) or information included:

13. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter
19. ☒ Certificate of Mailing by Express Mail
20. ☐ Other items or information:

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/807146	PCT/EP99/07518	29988/AX98115

21. The following fees are submitted:.

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

		CALCULATIONS PTO USE ONLY
☐	Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO	**$1,000.00**
☒	International preliminary examination fee (37 CFR 1.482) not paid to USPTO but Internation Search Report prepared by the EPO or JPO	**$860.00**
☐	International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	**$710.00**
☐	International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)	**$690.00**
☐	International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)	**$100.00**

ENTER APPROPRIATE BASIC FEE AMOUNT =	**$860.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).	**$0.00**	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	12 - 20 =	0	x $18.00	**$0.00**	
Independent claims	1 - 3 =	0	x $80.00	**$0.00**	
Multiple Dependent Claims **(check if applicable)**.			☐	**$0.00**	
TOTAL OF ABOVE CALCULATIONS			=	**$860.00**	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) **(check if applicable)**.			☐	**$0.00**	
SUBTOTAL			=	**$860.00**	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).			+	**$0.00**	
TOTAL NATIONAL FEE			=	**$860.00**	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) **(check if applicable).**			☐	**$0.00**	
TOTAL FEES ENCLOSED			=	**$860.00**	
				Amount to be: refunded	$
				charged	$

☒ A check in the amount of **$860.00** to cover the above fees is enclosed.

☐ Please charge my Deposit Account No. in the amount of to cover the above fees.
A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **13-2855** A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

James P. Zeller
Marshall, O'Toole, Gerstein, Murray & Borun
233 S. Wacker Drive
6300 Sears Tower
Chicago, IL 60606
(312) 616-6300

James A. Flight
SIGNATURE

James A. Flight
NAME

37,622
REGISTRATION NUMBER

April 6, 2001
DATE

PATENT APPLICATION

IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE

Applicants: Gallert et al. Serial No.: To be assigned Filed: Herewith (April 6, 2001) For: POLYGLUCAN AND POLYGLUCAN DERIVATIVES WHICH CAN BE OBTAINED FROM AMYLOSUCRASE BY BIOCATALYTIC PRODUCTION IN THE PRESENCE OF BIOGENIC SUBSTANCES Group Art Unit: To be assigned Examiner: To be assigned	"EXPRESS MAIL" mailing label No. EM564458605US. Date of Deposit: April 6, 2001 I hereby certify that this paper (or fee) is being deposited with the United States Postal Service "EXPRESS MAIL POST OFFICE TO ADDRESSEE" service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, Washington, D.C. 20231  Richard Zimmermann

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, DC 20231

Sir:

Please amend this application as follows.

IN THE SPECIFICATION:

Page 1 immediately following the title, please insert the following:

--This is the U.S. national phase of International Application No. PCT/EP99/07518 filed October 7, 1999, the

entire disclosure of which is incorporated herein by reference.--

IN THE ABSTRACT:

Please add an abstract as set forth on the attached sheet.

IN THE CLAIMS:

Please amend claims 1-12 as follows:

1. (Amended) A polyglucan or polyglucan derivative obtained from polyglucan sucrase or polyglucan amylosucrase in the presence of at least one member selected from the group consisting of transferase and glycosyltransferases.

2. (Amended) The polyglucan or polyglucan derivative as claimed in claim 1 having an amino acid sequence according to SEQ. ID. No. 1.

3. (Amended) The polyglucan derivative of claim 1, wherein the polyglucan derivative is a polyglucan ester or a polyglucan ether or a nature-identical polymer.

4. (Amended) The polyglucan derivative of claim 1, wherein the polyglucan derivative is a graft polymer, block polymer, copolymer, random copolymer or a starburst polymer, ladder polymer or band polymer.

5. (Amended) A process for producing polyglucans or polyglucan derivatives as claimed in claim 1, which comprises adding at least one transferase or at least one glycoside transferase to amylosucrase in vitro.

6. (Amended) An excipient comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

7. (Amended) A depot system for at least one active component having a therapeutic or prophylactic effect comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

8. (Amended) A pharmaceutical excipient or pharmaceutical tabletting aid comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

9. (Amended) An agrochemical carrier comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

10. (Amended) A cosmetic product comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

11. (Amended) A food or food additive comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

12. (Amended) A carrier for flavorings or fragrances comprising at least one polyglucan or polyglucan derivative as claimed in claim 1.

REMARKS

By the foregoing amendments to the specification, a cross-reference to the parent international application has been provided. The claims have been amended to better conform to U.S. practice and to omit multiple dependencies.

An abstract has been added.

The filing fee has been calculated based on the claims as amended above. No new matter has been added.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN, MURRAY & BORUN

April 6, 2001

By _____
James A. Flight
Reg. No. 37,622

6300 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606-6402
(312) 474-6300

CLAIMS IN AMENDED FORM

1. (Amended) A polyglucan [and/or] or polyglucan derivative [obtainable] obtained from polyglucan sucrase or polyglucan amylosucrase in the presence of at least one [transferase and/or one glycosyltransferase] member selected from the group consisting of transferase and glycosyltransferases.

2. (Amended) The [amylosucrase] polyglucan or polyglucan derivative as claimed in claim 1 having an amino acid sequence according to SEQ. ID. No. 1.

3. (Amended) The polyglucan derivative [as claimed in one of the preceding claims] of claim 1, wherein the polyglucan derivative is a polyglucan ester or a polyglucan ether or a nature-identical polymer.

4. (Amended) The polyglucan derivative [as claimed in one of the preceding claims] of claim 1, wherein the polyglucan derivative is a graft polymer, block polymer, copolymer, random copolymer or a starburst polymer, ladder polymer or band polymer.

5. (Amended) A process for producing polyglucans [and/or] or polyglucan derivatives as claimed in [claims 1-4] claim 1, which comprises adding at least one transferase [and/or] or at least one glycoside transferase [being added] to amylosucrase in vitro.

6. (Amended) [The use of] An excipient comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 for use as excipient].

7. (Amended) [The use of] A depot system for at least one active component having a therapeutic or prophylactic effect comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 as depot system for at least one active component having a therapeutic or prophylactic effect].

8. (Amended) [The use of] A pharmaceutical excipient or pharmaceutical tabletting aid comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 for the pharmaceutical sector, preferably excipient and/or tabletting aid].

9. (Amended) [The use of] An agrochemical carrier comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 for the agrochemical sector, preferably as carrier].

10. (Amended) [The use of] A cosmetic product comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 for cosmetic applications].

11. (Amended) [The use of] A food or food additive comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 as food and/or food additive].

12. (Amended) [The use of] A carrier for flavorings or fragrances comprising at least one polyglucan [and/or one] or polyglucan derivative as claimed in [claims] claim 1 [to 5 as carrier for flavorings and fragrances].

Polyglucan and polyglucan derivatives obtainable from amylosucrase biocatalytic production in the presence of biogenic substances

The invention relates to the production of polyglucan and polyglucan derivatives by recombinant amylosucrase in the presence of biogenic substances and a process for their production and use.

The biotechnology industry is interested in the production of novel biologically compatible substances and processes for their inexpensive production.

The production of unbranched polyglucans by biocatalytic production is described in WO 95/31553 with the use of recombinant amylosucrase. In the context of this invention, this publication is explicitly incorporated by reference. In particular, the recombinant amylosucrase described there exhibits the activity of native amylosucrase.

WO 95/31553 further describes the production of unbranched polysaccharides by means of biotransformation, the unbranched polysaccharide being produced by catalytic reaction of monomeric fundamental building blocks such as oligomeric saccharides, for example of mono- and/or disaccharides. In particular, poly(1,4-alpha-D-glucan) is synthesized in WO 95/31553 using a polysaccharide synthase, alpha-1,4-glycosyl-transferase or, synonymously, amylosucrase (EC 2.4.1.4). WO 95/31553 and PCT/EP98/05573 also disclose nucleic acid sequences which, in E. coli leads to a protein having the activity of an amylosucrase.

The unbranched polymers obtained biocatalytically in this manner in many applications have an advantage compared with branched polymers with respect to processability or special properties, for example

mechanical stability and stress-bearing capacity. Furthermore, in the pharmaceutical (human and veterinary sector), medical (human and veterinary sector), cosmetics or agrochemical sectors, there are applications of great commercial importance in which properties or combinations of properties are required which are either not obtained by unbranched polymers or their specific properties go beyond the extent required for the specific application for an application in the abovementioned, or other, fields of application. Achieving specific properties is associated with relatively high production costs. If these properties are not required in the application, this procedure must be avoided. Properties which do not necessarily require the use of unbranched polymers can be, for example, improved shapeability in the production of sample bodies of specific geometry, the porosity of sample bodies for general release of active materials of any type, in particular in the pharmaceutical sector and agrochemical sector, swellability, easier chemical modification on account of more readily accessible functional groups, etc.

Okada et al. (J. Biol. Chem. (1974), 249, 126) describes that in the presence of native amylosucrase containing impurities of dextrinyltransferase leads to specific branching in the molecule.

It is also known that primers affect the activity of native amylosucrase (see DE 19860376.2).

Surprisingly, it has been found that the activity of amylosucrase in the presence of biogenic substances, preferably other enzymes, is not impaired, but is rather advantageously increased in the context of production.

For industrial production, it is of importance to obtain economically valuable products. In addition, products are to be obtained which are biocompatible and can be used for numerous bioscience and material science applications. The advantage of such products is that they are suitable, inter alia, for use on and in living organisms, particularly in the human sector (cosmetics, foods, pharmaceuticals, medicine) and, owing to the biocompatability, the disposal after their use in industrial sectors is predominantly without problem.

Therefore, it is an object of the invention to use recombinant amylosucrase modified in biotechnological processes for the production of polyglucan and its derivatives in vitro and to obtain novel products. In vitro processes make it possible to produce reproducible products of the same quality and standards (see example).

The object according to the invention is achieved by using recombinant polyglucansucrase in the presence of biogenic substances, preferably enzymes, and is used for producing polyglucan and polyglucan derivatives.

Particular preference is given to those polyglucansucrases as disclosed in PCT/EP98/05573 (see SEQ. ID. No. 1). The invention therefore relates to an amylosucrase having the amino acid sequence SEQ. ID. No. 1 or a redundant variant.

In the context of this invention the term polyglucan and polyglucan derivatives encompass in particular amylose and amylose derivatives.

Of advantage here is the surprisingly high product uniformity of the resultant polyglucan and polyglucan derivatives, in particular of the molecular weights

achieved. Depending on the use of individual biogenic substances, in particular enzymes, very different polyglucans and/or polyglucan derivatives can be obtained; their molecular weight can vary from 10^3 to 10^9 daltons. Preferred molecular weights are in the range from 5×10^3 to 10^6 daltons, particularly preferably in the range 5×10^3 to 5×10^4 daltons.

The variety of the resultant products and their possible combinations is advantageous. From this, in particular in the case of a suitable combination of polymers with respect to their molecular weight and/or underlying primary structures, particular characteristics can be combined or the processability can be affected in a specific manner. This applies in particular to processing by processing methods of classical polymer chemistry, in particular in industrial applications.

The inventive polyglucans and polyglucan derivatives are further distinguished by a high variety which is determined by the polydispersity of the polyglucans and polyglucan derivatives. The polydispersity can be varied in broad ranges. For different applications quite different polydispersities are of interest. Polydispersity which is given by the quotient of polymer weight average and polymer number average can vary from 1.0 to 100 or more, polydispersities in the range from 1.1 to 15 being preferred for specific applications. Particularly advantageously, polyglucans or polyglucan derivatives which have polydispersities in the range from 1.1 to 5 are distinguished.

"Biocompatible" in the meaning of this invention means that the polysaccharides used are subjected to complete biodegradation and no harmful accumulation occurs in the food chain, in particular in the human organism.

Biodegradation here describes any process proceeding in vivo which leads to degradation or destruction of the polymer. In particular, hydrolytic or enzymatic processes also fall within this area. For the biocompatability of the polysaccharides and their breakdown products (metabolites), not least, the nature-identical character of the polysaccharides used is also of great importance. Therefore, the polysaccharides which come into consideration are also particularly suitable for therapeutic, diagnostic or prophylactic use.

In particular, increased yields of polyglucan and polyglucan derivatives can be obtained by using enzyme mixtures.

Advantageous enzymes which preferably come into consideration are, without the list below having the quality of completeness: transferases and glycosyl-transferases

2.4.1.1 Phosphorylase.
2.4.1.2 Dextrin dextranase.
2.4.1.5 Dextransucrase.
2.4.1.7 Sucrose phosphorylase.
2.4.1.8 Maltose phosphorylase.
2.4.1.9 Inulosucrase.
2.4.1.10 Levansucrase.
2.4.1.11 Glycogen (starch) synthase.
2.4.1.12 Cellulose synthase (UDP-forming).
2.4.1.13 Sucrose synthase.
2.4.1.14 Sucrose-phosphate synthase.
2.4.1.15 Alpha,alpha-trehalose-phosphate synthase (UDP-forming).
2.4.1.16 Chitin synthase.
2.4.1.17 UDP-glucuronosyltransferase.
2.4.1.18 1,4-alpha-glucan branching enzyme.
2.4.1.19 Cyclomaltodextrin glucanotransferase.

2.4.1.20 Cellobiose phosphorylase.
2.4.1.21 Starch (bacterial glycogen) synthase.
2.4.1.22 Lactose synthase.
2.4.1.23 Sphingosine beta-galactosyltransferase.
2.4.1.24 1,4-alpha-glucan-6-alpha-glucosyltransferase.
2.4.1.25 4-alpha-glucanotransferase.
2.4.1.26 DNA alpha-glucosyltransferase.
2.4.1.27 DNA beta-glucosyltransferase.
2.4.1.28 Glucosyl-DNA beta-glucosyltransferase.
2.4.1.29 Cellulose synthase (GDP-forming).
2.4.1.30 1,3-beta-oligoglucan phosphorylase.
2.4.1.31 Laminaribiose phosphorylase.
2.4.1.32 Glucomannan 4-beta-mannosyltransferase.
2.4.1.33 Alginate synthase.
2.4.1.34 1,3-beta-glucan synthase.
2.4.1.35 Phenol beta-glucosyltransferase.
2.4.1.36 Alpha,alpha-trehalose-phosphate synthase (GDP-forming).
2.4.1.37 Glycoprotein-fucosylgalactoside alpha-galactosyltransferase.
2.4.1.38 Beta-N-acetylglucosaminyl-glycopeptide beta-1,4-galactosyltransferase.
2.4.1.39 Steroid N-acetylglucosaminyltransferase.
2.4.1.40 Glycoprotein-fucosylgalactoside alpha-N-acetylgalactosaminyltransferase.
2.4.1.41 Polypeptide N-acetylgalactosaminyl-transferase.
2.4.1.43 Polygalacturonate-4-alpha-galacturonosyl-transferase.
2.4.1.44 Lipopolysaccharide galactosyltransferase.
2.4.1.45 2-hydroxyacylsphingosine-1-beta-galactosyl-transferase.
2.4.1.46 1,2-diacylglycerol-3-beta-galactosyl-transferase.
2.4.1.47 N-acylsphingosine galactosyltransferase.
2.4.1.48 Heteroglycan alpha-mannosyltransferase.
2.4.1.49 Cellodextrin phosphorylase.
2.4.1.50 Procollagen galactosyltransferase.

2.4.1.52 Poly(glycerol-phosphate) alpha-glucosyltransferase.
2.4.1.53 Poly(ribitol-phosphate) beta-glucosyltransferase.
2.4.1.54 Undecaprenyl-phosphate mannosyltransferase.
2.4.1.55 Transferred entry: 2.7.8.14.
2.4.1.56 Lipopolysaccharide N-acetylglucosaminyltransferase.
2.4.1.57 Phosphatidyl-myo-inositol alpha-mannosyltransferase.
2.4.1.58 Lipopolysaccharide glucosyltransferase I.
2.4.1.60 Abequosyltransferase.
2.4.1.62 Ganglioside galactosyltransferase.
2.4.1.63 Linamarin synthase.
2.4.1.64 Alpha,alpha-trehalose phosphorylase.
2.4.1.65 Galactoside 3(4)-L-fucosyltransferase.
2.4.1.66 Procollagen glucosyltransferase.
2.4.1.67 Galactinol-raffinose galactosyltransferase.
2.4.1.68 Glycoprotein 6-alpha-L-fucosyltransferase.
2.4.1.69 Galactoside 2-L-fucosyltransferase.
2.4.1.70 Poly(ribitol-phosphate) N-acetylglucosaminyltransferase.
2.4.1.71 Arylamine glucosyltransferase.
2.4.1.72 Transferred entry: 2.4.2.24.
2.4.1.73 Lipopolysaccharide glucosyltransferase II.
2.4.1.74 Glycosaminoglycan galactosyltransferase.
2.4.1.75 UDP-galacturonosyltransferase.
2.4.1.78 Phosphopolyprenol glucosyltransferase.
2.4.1.79 Galactosylgalactosylglucosylceramide beta-D-acetyl-galactoaminyltransferase
2.4.1.80 Ceramide glucosyltransferase.
2.4.1.81 Flavone 7-O-beta-glucosyltransferase.
2.4.1.82 Galactinol-sucrose galactosyltransferase.
2.4.1.83 Dolichyl-phosphate beta-D-mannosyltransferase.
2.4.1.85 Cyanohydrin beta-glucosyltransferase.
2.4.1.86 Glucosaminylgalactosylglucosylceramide beta-galactosyltransferase.

2.4.1.87 Beta-galactosyl-N-acetylglucosaminyl-glycopeptide alpha-1,3-galactosyltransferase.

2.4.1.88 Globoside alpha-N-acetylgalactosaminyl-transferase.

2.4.1.90 N-acetyllactosamine synthase.

2.4.1.91 Flavonol 3-O-glucosyltransferase.

2.4.1.92 (N-acetylneuraminyl)-galactosylglucosyl-ceramide N-acetylgalactosaminyltransferase.

2.4.1.93 Inulin fructotransferase (depolymerizing).

2.4.1.94 Protein N-acetylglucosaminyltransferase.

2.4.1.95 Bilirubin-glucuronoside glucuronosyl-transferase.

2.4.1.96 Sn-glycerol-3-phosphate 1-galactosyl-transferase.

2.4.1.97 1,3-beta-glucan phosphorylase.

2.4.1.99 Sucrose 1F-fructosyltransferase.

2.4.1.100 1,2-beta-fructan 1F-fructosyltransferase.

2.4.1.101 Alpha-1,3-mannosyl-glycoprotein beta-1,2-N-acetylglucosaminyltransferase.

2.4.1.102 Beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,6-N-acetylglucosaminyltransferase.

2.4.1.103 Alizarin 2-beta-glucosyltransferase.

2.4.1.104 O-dihydroxycoumarin 7-O-glucosyltransferase.

2.4.1.105 Vitexin beta-glucosyltransferase.

2.4.1.106 Isovitexin beta-glucosyltransferase.

2.4.1.109 Dolichyl-phosphate-mannose-protein mannosyl-transferase.

2.4.1.110 tRNA-queuosine beta-mannosyltransferase.

2.4.1.111 Coniferyl-alcohol glucosyltransferase.

2.4.1.112 Alpha-1,4-glucan-protein synthase (UDP-forming).

2.4.1.113 Alpha-1,4-glucan-protein synthase (ADP-forming).

2.4.1.114 2-coumarate O-beta-glucosyltransferase.

2.4.1.115 Anthocyanidin 3-O-glucosyltransferase.

2.4.1.116 Cyanidin-3-rhamnosylglucoside 5-O-glucosyl-transferase.

2.4.1.117 Dolichyl-phosphate beta-glucosyltransferase.

2.4.1.118 Cytokinin 7-beta-glucosyltransferase.
2.4.1.119 Dolichyl-diphosphooligosaccharide-protein glycosyltransferase.
2.4.1.120 Sinapate 1-glucosyltransferase.
2.4.1.121 Indole-3-acetate beta-glucosyltransferase.
2.4.1.122 Glycoprotein-N-acetylgalactosamine 3-beta-galactosyltransferase.
2.4.1.123 Inositol 1-alpha-galactosyltransferase.
2.4.1.124 N-acetyllactosamine 3-alpha-galactosyltransferase.
2.4.1.125 Sucrose-1,6-alpha-glucan 3(6)-alpha-glucosyltransferase.
2.4.1.126 Hydroxycinnamate 4-beta-glucosyltransferase.
2.4.1.127 Monoterpenol beta-glucosyltransferase.
2.4.1.128 Scopoletin glucosyltransferase.
2.4.1.129 Peptidoglycan glycosyltransferase.
2.4.1.130 Dolichyl-phosphate-mannose-glycolipid alpha-mannosyltransferase.
2.4.1.131 Glycolipid 2-alpha-mannosyltransferase.
2.4.1.132 Glycolipid 3-alpha-mannosyltransferase.
2.4.1.133 Xylosylprotein 4-beta-galactosyltransferase.
2.4.1.134 Galactosylxylosylprotein 3-beta-galactosyltransferase.
2.4.1.135 Galactosylgalactosylxylosylprotein 3-beta-glucuronosyltransferase.
2.4.1.136 Gallate 1-beta-glucosyltransferase.
2.4.1.137 Sn-glycerol-3-phosphate 2-alpha-galactosyltransferase.
2.4.1.138 Mannotetraose 2-alpha-N-acetylglucosaminyltransferase.
2.4.1.139 Maltose synthase.
2.4.1.140 Alternansucrase.
2.4.1.141 N-acetylglucosaminyldiphosphodolichol N-acetylglucosaminyltransferase.
2.4.1.142 Chitobiosyldiphosphodolichol alpha-mannosyltransferase.
2.4.1.143 Alpha-1,6-mannosyl-glycoprotein beta-1,2-N-acetylglucosaminyltransferase.

2.4.1.144 Beta-1,4-mannosyl-glycoprotein beta-1,4-N-acetylglucosaminyltransferase.

2.4.1.145 Alpha-1,3-mannosyl-glycoprotein beta-1,4-N-acetylglucosaminyltransferase.

2.4.1.146 Beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,3-N-acetylglucosaminyltransferase.

2.4.1.147 Acetylgalactosaminyl-O-glycosyl-glycoprotein beta-1,3-N-acetylglucosaminyltransferase.

2.4.1.148 Acetylgalactosaminyl-O-glycosyl-glycoprotein beta-1,6-N-acetylglucosaminyltransferase.

2.4.1.149 N-acetyllactosaminide beta-1,3-N-acetylglucosaminyltransferase.

2.4.1.150 N-acetyllactosaminide beta-1,6-N-acetylglucosaminyltransferase.

2.4.1.151 N-acetyllactosaminide alpha-1,3-galactosyltransferase.

2.4.1.152 Galactoside 3-fucosyltransferase.

2.4.1.153 Dolichyl-phosphate alpha-N-acetylglucosaminyltransferase.

2.4.1.154 Globotriosylceramide beta-1,6-N-acetylgalactosaminyltransferase.

2.4.1.155 Alpha-1,3(6)-mannosylglycoprotein beta-1,6-N-acetyl-glucosaminyltransferase.

2.4.1.156 Indolylacetyl-myo-inositol galactosyltransferase.

2.4.1.157 1,2-diacylglycerol 3-glucosyltransferase.

2.4.1.158 13-hydroxydocosanoate 13-beta-glucosyltransferase.

2.4.1.159 Flavonol-3-O-glucoside L-rhamnosyltransferase.

2.4.1.160 Pyridoxine 5'-O-beta-D-glucosyltransferase.

2.4.1.161 Oligosaccharide 4-alpha-D-glucosyltransferase.

2.4.1.162 Aldose beta-D-fructosyltransferase.

2.4.1.163 Beta-galactosyl-N-acetylglucosaminyl-galactosyl-glucosylceramide beta-1,3-acetylglucosaminyltransferase.

2.4.1.164 Galactosyl-N-acetylglucosaminylgalactosyl-glucosylceramide beta-1,6-N-acetylglucosaminyltransferase.

2.4.1.165 N-acetylneuraminylgalactosylglucosylceramide beta-1,4-N-acetylgalactosaminyltransferase.

2.4.1.166 Raffinose-raffinose alpha-galactosyltransferase.

2.4.1.167 Sucrose 6(F)-alpha-galactosyltransferase.

2.4.1.168 Xyloglucan 4-glucosyltransferase.

2.4.1.169 Xyloglucan 6-xylosyltransferase.

2.4.1.170 Isoflavone 7-O-glucosyltransferase.

2.4.1.171 Methyl-ONN-azoxymethanol glucosyltransferase.

2.4.1.172 Salicyl-alcohol glucosyltransferase.

2.4.1.173 Sterol glucosyltransferase.

2.4.1.174 Glucuronylgalactosylproteoglycan beta-1,4-N-acetylgalactosaminyltransferase.

2.4.1.175 Glucuronyl-N-acetylgalactosaminylproteoglycan beta-1,4-N-acetylgalactosaminyltransferase.

2.4.1.176 Gibberellin beta-glucosyltransferase.

2.4.1.177 Cinnamate glucosyltransferase.

2.4.1.178 Hydroxymandelonitrile glucosyltransferase.

2.4.1.179 Lactosylceramide beta-1,3-galactosyltransferase.

2.4.1.180 Lipopolysaccharide N-acetylmannosaminouronosyltransferase.

2.4.1.181 Hydroxyanthraquinone glucosyltransferase.

2.4.1.182 Lipid-A-disaccharide synthase.

2.4.1.183 Alpha-1,3-glucan synthase.

2.4.1.184 Galactolipid galactosyltransferase.

2.4.1.185 Flavonone 7-O-beta-glucosyltransferase.

2.4.1.186 Glycogenin glucosyltransferase.

2.4.1.187 N-acetylglucosaminyldiphosphoundecaprenol N-acetyl-beta-D-mannosaminyltransferase.

2.4.1.188 N-acetylglucosaminyldiphosphoundecaprenol glucosyltransferase.

2.4.1.189 Luteolin 7-O-glucoronosyltransferase.

2.4.1.190 Luteolin 7-O-glucoronide 7-O-glucoronosyltransferase.

2.4.1.191 Luteolin 7-O-diglucoronide 4'-O-glucoronosyltransferase.
2.4.1.192 Nuatigenin 3-beta-glucosyltransferase.
2.4.1.193 Sarsapogenin 3-beta-glucosyltransferase.
2.4.1.194 4-hydroxybenzoate 4-O-beta-D-glucosyltransferase.
2.4.1.195 Thiohydroximate beta-D-glucosyltransferase.
2.4.1.196 Nicotinate glucosyltransferase.
2.4.1.197 High-mannose-oligosaccharide beta-1,4-N-acetylglucosaminyltransferase.
2.4.1.198 Phosphatidylinositol N-acetylglucosaminyltransferase.
2.4.1.199 Beta-mannosylphosphodecaprenol-mannooligosaccharide 6-mannosyltransferase.
2.4.1.200 Inulin fructotransferase (depolymerizing, difructofuranose-1,2':2',1-dianhydride-forming).
2.4.1.201 Mannosyl-glycoprotein beta-1,4-N-acetylglucosaminyltransferase.
2.4.1.202 2,4-hydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-one 2-D-glucosyltransferase.
2.4.1.203 Zeatin O-beta-D-glucosyltransferase.
2.4.1.204 Zeatin O-beta-D-xylosyltransferase.
2.4.1.205 Galactogen 6-beta-galactosyltransferase.
2.4.1.206 Lactosylceramide 1,3-N-acetyl-beta-D-glucosaminyltransferase.
2.4.1.207 Xyloglucan:xyloglucosyltransferase.
2.4.1.208 Diglucosyl diacylglycerol (DGlcDAG) synthase.
2.4.2.1 Purine-nucleoside phosphorylase.
2.4.2.2 Pyrimidine-nucleoside phosphorylase.
2.4.2.3 Uridine phosphorylase.
2.4.2.4 Thymidine phosphorylase.
2.4.2.5 Nucleoside ribosyltransferase.
2.4.2.6 Nucleoside deoxyribosyltransferase.
2.4.2.7 Adenine phosphoribosyltransferase.
2.4.2.8 Hypoxanthine phosphoribosyltransferase.
2.4.2.9 Uracil phosphoribosyltransferase.
2.4.2.10 Orotate phosphoribosyltransferase.

2.4.2.11 Nicotinate phosphoribosyltransferase.
2.4.2.12 Nicotinamide phosphoribosyltransferase.
2.4.2.13 Transferred entry: 2.5.1.6.
2.4.2.14 Amidophosphoribosyltransferase.
2.4.2.15 Guanosine phosphorylase.
2.4.2.16 Urate-ribonucleotide phosphorylase.
2.4.2.17 ATP phosphoribosyltransferase.
2.4.2.18 Anthranilate phosphoribosyltransferase.
2.4.2.19 Nicotinate-nucleotide pyrophosphorylase (carboxylating).
2.4.2.20 Dioxotetrahydropyrimidine phosphoribosyltransferase.
2.4.2.21 Nicotinate-nucleotide-dimethylbenzimidazole phosphoribosyltransferase.
2.4.2.22 Xanthine-guanine phosphoribosyltransferase.
2.4.2.23 Deoxyuridine phosphorylase.
2.4.2.24 1,4-beta-D-xylan synthase.
2.4.2.25 Flavone apiosyltransferase.
2.4.2.26 Protein xylosyltransferase.
2.4.2.27 dTDP-dihydrostreptose-streptidine-6-phosphate dihydrostreptosyltransferase.
2.4.2.28 5'-methylthioadenosine phosphorylase.
2.4.2.29 Queuine tRNA-ribosyltransferase.
2.4.2.30 NAD(+)ADP-ribosyltransferase.
2.4.2.31 NAP(p)(+)-arginine ADP-ribosyltransferase.
2.4.2.32 Dolichyl-phosphate D-xylosyltransferase.
2.4.2.33 Dolichyl-xylosyl-phosphate-protein xylosyltransferase.
2.4.2.34 Indolylacetylinositol arabinosyltransferase.
2.4.2.35 Flavonol-3-O-glycoside xylosyltransferase.
2.4.2.36 NAD(+)-diphthamide ADP-ribosyltransferase.
2.4.2.37 NAD(+)-dinitrogen-reductase ADP-D-ribosyltransferase.
2.4.99.1 Beta-galactosamide alpha-2,6-sialyltransferase.
2.4.99.2 Monosialoganglioside sialyltransferase.
2.4.99.3 Alpha-N-acetylgalactosaminide alpha-2,6-sialyltransferase.

2.4.99.4 Beta-galactoside alpha-2,3-sialyltransferase.
2.4.99.5 Galactosyldiacylglycerol alpha-2,3-sialyltransferase.
2.4.99.6 N-acetyllactosaminide alpha-2,3-sialyltransferase.
2.4.99.7 (Alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase.
2.4.99.8 Alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase.
2.4.99.9 Lactosylceramide alpha-2,3-sialyltransferase.
2.4.99.10 Neolactotetraosylceramide alpha-2,3-sialyltransferase.
2.4.99.11 Lactosylceramide alpha-2,6-N-sialyltransferase.

The invention therefore relates to the inexpensive derivatization of polyglucan.

Derivatization, for the purposes of this invention, means that the functional groups naturally occurring in polyglucan, hydroxyl groups (also: alcohol functions), are derivatized, replaced, modified or chemically substituted. Derivatization is therefore also taken to mean the introduction of branches by means of biogenic substances, in particular said enzymes.

Derivatives for the purposes of these inventions are also those which undergo a reaction specifically of one of the C atoms C-2, C-2 or C-6 more precisely from > 0% to a maximum of 100%, or mixtures occur, that is to say different percentage derivatizations at different positions in the C-6 body of a glucan unit. In the case of the hydroxyl group on the C-6 atom of the glucan building block in the polyglucan, in particular advantageous degrees of branching of 1% to 40% can be obtained. In particular, these polyglucan derivatives are distinguished by degrees of branching of 2% to 10%.

In particular the type of branching and the number of branches in the described polyglucan derivatives are distinguished by their being able to differ from natural polyglucans, that is to say polyglucans occurring in nature, as can be produced from plants, animals or other organisms.

The invention therefore also relates to the modified production of polyglucan by means of biogenic substances. This means in the context of this invention the addition of biogenic substances as early as during the expression of the amylosucrase with subsequent biotransformation and synthesis of the polyglucans or polyglucan derivatives and/or the post-treatment by means of biogenic substances of such products produced.

In particular, mixtures of amylosucrase or other enzymes which synthesize polyglucans and are known to those skilled in the art in the presence of other molecules having enzymatic activity or neutral behavior with respect to the reaction to form polyglucans, but which have a positive effect on the reaction (below and above "biogenic substances"). In the broadest sense these are to be taken to mean biotic substances which are used by biological organisms or affect them, in particular in metabolic processes. These improvements are: yield increases, digestion of by-products (for example resultant fructose, whose breakdown products serve as a quasi nutrient medium for further polyglucan synthesis) and other reaction parameters known for the enzymatic reaction which are known to those skilled in the art in the field of enzymatic reactions.

- "biogenic" substances can also be those which preferably have the following elements: C, H, O, N, P, S, B, Si, Se, alkali metals, alkaline earth metals, halogens, Co, Fe, Hg,

and/or

have functional bonds which are different from carbon-hydrogen bonds, such as: amide, phosphate, sulfate, carboxyl, hydroxyl, carbonyl, carbamyl, urea, urethane, ester, ether, lactone, lactam,

and/or

- have classes of substances such as peptides, proteins, enzymes, nucleotides and nucleic acids and other classes of substances known to those skilled in the art, classified within the meaning of organic chemistry

and/or

- a compound which has an advantageous biological activity in biological organisms.

To this extent, by means of the invention described, the following derivatives can be obtained, without the enumeration being complete

A) Polyglucan esters
acetates
nitrates
phosphates
xanthogenates
citrates

B) Polyglucan ethers
hydroxyethyl
hydroxypropyl
1,2-dihydroxypropyl
carboxymethyl

C) Products of polyglucan breakdown by oxidation or partial ring opening
dialdehyde amylose
carboxy amylose
persulfate of broken-down polyglucan

D) Natural polymers (nature-identical polymers/polyglucans)
amylopectin
glycogen
and/or graft polymers, block polymers, copolymers, random copolymers, alternating copolymers and dendritic copolymers, including starburst polymers and ladder polymers, and also band polymers.

The term copolymer within the meaning of this invention encompasses polyglucan and/or polyglucan derivatives from two or more fundamental units (monomers).

For the subject matter of the invention, it is critical either to carry out said biotransformation in modified form or to modify the resultant polyglucan product after polymerization has been carried out in a second reaction, preferably a biocatalysis. This is achieved by isolating the polyglucan or polyglucan derivative as far as possible from all reaction partners/parameters of biotransformation and further modifying it in a further reaction. This can be performed by using the addition of further biogenic compounds, preferably enzymes.

Another classification of the various reaction paths for producing polyglucans and/or polyglucan derivatives can be described as follows.

The modification of the polyglucans or polyglucan derivatives can be carried out according to whether only the reaction course of the biotransformation, that

is to say the reaction of sucrose and its derivatives to form polyglucan and/or polyglucan derivatives is to be modified (this can occur, for example, by consuming the fructose formed in the biotransformation), or a polyglucan and/or one or more polyglucan derivatives can be formed directly by the reaction or reaction procedure in the reaction of amylosucrase with biogenic substances. In this case the one does not exclude the other. An example which may be mentioned here is the altered reaction course which results from obtaining, by phosphorylation and/or methylation and/or sulfation and/or further modifications, an increased or reduced solubility of the polyglucan and in this manner obtaining, for example, altered chain lengths or the like.

In addition, other modifying enzymes can be coded for, for example, in the same operon as the amylosucrase, and can be purified in parallel with this enzyme. In this manner as early as during the production and separation of the amylosucrase a mix is formed of different biogenic substances, preferably different enzymes including amylosucrase, which can be used in biocatalysis (biotransformation).

Such mixtures are also known to those skilled in the art under the name "polymer blends". For example, amylosucrases modified in this manner can cause sugars, monosaccharides, disaccharides, oligosaccharides which are varied in their chemical structure being incorporated better into the polymer structure, in the context of a more rapid reaction or in the context of a higher compatability with other monomeric sugar units which are incorporated into the polymer backbone. However, chain breaking, which can lead to specific functional molecules owing to their special polymer end groups which have particular properties, for example surface-active behavior, in the broadest sense of

amphiphilic molecules, is not to be excluded and can even become the preferred reaction.

The polyglucans which are enzymatically modified by the use of biogenic compounds can be used as starting material for further chemical modifications.

The invention further relates to the use of the inventively obtained polyglucans and/or polyglucan derivatives, as follows:
use as pharmaceutical formulation and/or agrochemical formulation for application in agriculture (as tablet, capsule constituent, suspensions, emulsions and other formulations known to those skilled in the art in said fields), carriers and/or depot formulation, in particular tabletting aid, use as food and/or food additive, use as cosmetic additive. These advantageous uses of the inventive polyglucans are due to the provision of biocompatability by the inventive use of biogenic substances.

Active compounds within the meaning of this invention are preferably all compounds which have a palliative or curative effect for a biological organism, in particular human, animal, plant. The term active compounds in the general meaning also includes agrochemical compounds having fungicidal, pesticidal, insecticidal or herbicidal effect, but also, in general, those compounds which have a useful effect in agriculture, forestry or horticulture, for example fertilizers. Fragrances or flavorings which are used in particular in the food sector or cosmetics also come under the term active compound. To this extent, all active compounds are also explicitly included which have a therapeutic and/or prophylactic and/or decorative effect.

Examples

Description of the most important sequences:
SEQ ID No. 1 describes an amino acid sequence having the activity of an amylosucrase obtainable by recombination technology in E. coli from a DNA of the organism Neisseira polysaccharea and as demonstrated in WO 95/31553 and PCT/EP 98/05573.

Example 1:
Mixing amylosucrase and another enzyme having a different activity leads to a derivatized amylose product, as follows: an example is here the mixing of amylosucrase with amylo-1,4→1,4-transglycosylase. This enzyme catalyzes the introduction of 1,6 branches into unbranched amylose molecules having a minimum length of 6-11 glucose units. This size range is precisely in the range of the glucose polymers produced by the amylosucrase. This thus produces a highly branched but very short-chain molecule.
To carry out the experiment 200 U of recombinant amylosucrase are added to 2 g of D-glucose and 0.02% NaN_3 in a 10 ml volume of 50 mM Na citrate buffer having a pH of 6.5. In addition, 10 U of the amylo-1,4→1,6-transglycosylase are added to the solution. The solution is incubated at 37°C for 72 h without mixing. The resultant products are precipitated with ethanol and analyzed via GPC. Under said conditions, about 0.75 g of polymeric product having a degree of branching of 10% is produced.

Patent claims:

1. A polyglucan and/or polyglucan derivative obtainable from polyglucan sucrase or amylosucrase in the presence of at least one transferase and/or one glycosyltransferase.

2. The amylosucrase as claimed in claim 1 having an amino acid sequence according to SEQ ID. No. 1.

3. The polyglucan derivative as claimed in one of the preceding claims, wherein the polyglucan derivative is a polyglucan ester or a polyglucan ether or a nature-identical polymer.

4. The polyglucan derivative as claimed in one of the preceding claims, wherein the polyglucan derivative is a graft polymer, block polymer, copolymer, random copolymer or a starburst polymer, ladder polymer or band polymer.

5. A process for producing polyglucans and/or polyglucan derivatives as claimed in claims 1-4, which comprises at least one transferase and/or one glycoside transferase being added to amylosucrase in vitro.

6. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5 for use as excipient.

7. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5 as depot system for at least one active component having a therapeutic or prophylactic effect.

8. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5

for the pharmaceutical sector, preferably excipient and/or tabletting aid.

9. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5 for the agrochemical sector, preferably as carrier.

10. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5 for cosmetic applications.

11. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5 as food and/or food additive.

12. The use of at least one polyglucan and/or one polyglucan derivative as claimed in claims 1 to 5 as carrier for flavorings and fragrances.

ABSTRACT

The invention relates to polyglucans and polyglucan derivatives which can be produced from polyglucan sucrase or from amylosucrase by biocatalytic production in the presence of biogenic substances. The invention also relates to a method for the production thereof and to their use.

DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name; I believe that I am an original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled **"POLYGLUCAN AND POLYGLUCAN DERIVATIVES WHICH CAN BE OBTAINED FROM AMYLOSUCRASE BY BIOCATALYTIC PRODUCTION IN THE PRESENCE OF BIOGENIC SUBSTANCES,"** the specification of which was filed on October 7, 1999, as Application Serial No. 09/807,146 and was amended on April 6, 2001. I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment(s) referred to above. I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in 37 C.F.R. §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

			Priority Claimed	
19846492.4	Germany	9 October 1998	☒	☐
(Application Serial Number)	(Country)	(Day/Month/Year Filed)	Yes	No

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below:

(Application Serial Number)	(Day/Month/Year Filed)

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) or international (PCT) application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior application(s) in the manner provided by the first paragraph of 35 U.S.C. §112, lacknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in 37 C.F.R. §1.56 which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PCT/EP99/07518	7 October 1999	Pending
(Application Serial Number)	(Day/Month/Year Filed)	(Status-Patented, Pending or Abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY [redacted] hereby appoint as my attorneys, with full powe[redacted] substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

John B. Lungmus(18,566)	Patrick D. Ertel (26,877)	James J. Napoli (32,361)	James A. Flight (37,622)
Allen H. Gerstein (22,218)	Richard B. Hoffman(26,910)	Richard M. La Barge (32,254)	Roger A. Heppermann (37,641)
Nate F. Scarpelli (22,320)	James P. Zeller (28,491)	Li-Hsien Rin-Laures, M.D. (33,547)	David A. Gass (38,153)
Michael F. Borun (25,447)	Kevin D. Hogg (31,839)	Douglass C. Hochstetler (33,710)	Gregory C. Mayer (38,238)
Trevor B. Joike (25,542)	Jeffrey S. Sharp (31,879)	Robert M. Gerstein (34,824)	Michael R. Weiner (38,359)
Carl E. Moore, Jr. (26,487)	Martin J. Hirsch (32,237)	Anthony G. Sitko (36,278)	William K. Merkel (40,725)
Richard H. Anderson (26,526)		25	

Send correspondence to: James P. Zeller

FIRM NAME	PHONE NO.	STREET	CITY & STATE	ZIP CODE
Marshall, Gerstein & Borun	312-474-6300	6300 Sears Tower 233 South Wacker Drive	Chicago, Illinois	60606-6402

Full Name of First or Sole Inventor Karl-Christian Gallert	Citizenship Germany
Residence Address - Street ~~Rendeler Strasse 91~~ KARL-LIEBKNECHT-STR. 25	Post Office Address - Street ~~Rendeler Strasse 91~~ KARL-LIEBKNECHT-STR 25
City (Zip) D-61184 Karben	City (Zip) D-61184 Karben
State or Country Germany	State or Country Germany
Date ☒ OCTOBER 11, 2001	Signature ☒

Full Name of First or Sole Inventor Holger Bengs	Citizenship Germany
Residence Address - Street Bindingstrasse 3	Post Office Address - Street Bindingstrasse 3
City (Zip) D-60598 Frankfurt am Main	City (Zip) D-60598 Frankfurt am Main
State or Country Germany	State or Country Germany
Date ☒	Signature ☒

Second Joint Inventor, if any Claus Simandi	Citizenship Germany
Residence Address - Street Sossenheimer Mühlgasse 10	Post Office Address - Street Sossenheimer Mühlgasse 10
City (Zip) D-65936 Frankfurt an Main	City (Zip) D-65936 Frankfurt an Main
State or Country Germany	State or Country Germany
Date ☒	Signature ☒

APPLICABLE RULES AND STATUTES

37 CFR 1.56. DUTY OF DISCLOSURE - INFORMATION MATERIAL TO PATENTABILITY (Applicable Portion)

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is canceled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability of a claim that is canceled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§ 1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application, and
(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentability defines, to make sure that any material information contained therein is disclosed to the Office.

Information relating to the following factual situations enumerated in 35 USC 102 and 103 may be considered material under 37 CFR 1.56(a).

35 U.S.C. 102. CONDITIONS FOR PATENTABILITY: NOVELTY AND LOSS OF RIGHT TO PATENT

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraph (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent, or

(f) he did not himself invent the subject matter sought to be patented, or

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. 103. CONDITIONS FOR PATENTABILITY; NON-OBVIOUS SUBJECT MATTER (Applicable Portion)

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

35 U.S.C. 112. SPECIFICATION (Applicable Portion)

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name; I believe that I am an original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled **"POLYGLUCAN AND POLYGLUCAN DERIVATIVES WHICH CAN BE OBTAINED FROM AMYLOSUCRASE BY BIOCATALYTIC PRODUCTION IN THE PRESENCE OF BIOGENIC SUBSTANCES,"** the specification of which was filed on October 7, 1999, as Application Serial No. 09/807,146 and was amended on April 6, 2001. I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment(s) referred to above. I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in 37 C.F.R. §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

			Priority Claimed	
19846492.4	Germany	9 October 1998	☒	☐
(Application Serial Number)	(Country)	(Day/Month/Year Filed)	Yes	No

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below:

(Application Serial Number)	(Day/Month/Year Filed)

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) or international (PCT) application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior application(s) in the manner provided by the first paragraph of 35 U.S.C. §112, lacknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in 37 C.F.R. §1.56 which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PCT/EP99/07518	7 October 1999	Pending
(Application Serial Number)	(Day/Month/Year Filed)	(Status-Patented, Pending or Abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY. I hereby appoint as my attorneys, with full powers of substitution and revocation, to prosecute this application and transact all bus[illegible]s in the Patent and Trademark Office conne[illegible] therewith.

John B. Lungmus(18,566)	Patrick D. Ertel (26,877)	James J. Napoli (32,361)	James A. Flight (37,622)
Allen H. Gerstein (22,218)	Richard B. Hoffman(26,910)	Richard M. La Barge (32,254)	Roger A. Heppermann (37,641)
Nate F. Scarpelli (22,320)	James P. Zeller (28,491)	Li-Hsien Rin-Laures, M.D. (33,547)	David A. Gass (38,153)
Michael F. Borun (25,447)	Kevin D. Hogg (31,839)	Douglass C. Hochstetler (33,710)	Gregory C. Mayer (38,238)
Trevor B. Joike (25,542)	Jeffrey S. Sharp (31,879)	Robert M. Gerstein (34,824)	Michael R. Weiner (38,359)
Carl E. Moore, Jr. (26,487)	Martin J. Hirsch (32,237)	Anthony G. Sitko (36,278)	William K. Merkel (40,725)
Richard H. Anderson (26,526)			

Send correspondence to: James P. Zeller

FIRM NAME	PHONE NO.	STREET	CITY & STATE	ZIP CODE
Marshall, Gerstein & Borun	312-474-6300	6300 Sears Tower 233 South Wacker Drive	Chicago, Illinois	60606-6402

Full Name of First or Sole Inventor Karl-Christian Gallert	Citizenship Germany
Residence Address - Street Rendeler Strasse 91	Post Office Address - Street Rendeler Strasse 91
City (Zip) D-61184 Karben	City (Zip) D-61184 Karben
State or Country Germany	State or Country Germany
Date ☒	Signature ☒

Full Name of First or Sole Inventor Holger Bengs	Citizenship Germany
Residence Address - Street Bindingstrasse 3	Post Office Address - Street Bindingstrasse 3
City (Zip) D-60598 Frankfurt am Main	City (Zip) D-60598 Frankfurt am Main
State or Country Germany	State or Country Germany
Date ☒ 29.8.2001	Signature ☒

Second Joint Inventor, if any Claus Simandi	Citizenship Germany
Residence Address - Street Sossenheimer Mühlgasse 10	Post Office Address - Street Sossenheimer Mühlgasse 10
City (Zip) D-65936 Frankfurt an Main	City (Zip) D-65936 Frankfurt an Main
State or Country Germany	State or Country Germany
Date ☒	Signature ☒

APPLICABLE RULES AND STATUTES

37 CFR 1.56. DUTY OF DISCLOSURE - INFORMATION MATERIAL TO PATENTABILITY (Applicable Portion)

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is canceled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability of a claim that is canceled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§ 1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application, and
(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentability defines, to make sure that any material information contained therein is disclosed to the Office.

Information relating to the following factual situations enumerated in 35 USC 102 and 103 may be considered material under 37 CFR 1.56(a).

35 U.S.C. 102. CONDITIONS FOR PATENTABILITY: NOVELTY AND LOSS OF RIGHT TO PATENT

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraph (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent, or

(f) he did not himself invent the subject matter sought to be patented, or

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. 103. CONDITIONS FOR PATENTABILITY; NON-OBVIOUS SUBJECT MATTER (Applicable Portion)

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

35 U.S.C. 112. SPECIFICATION (Applicable Portion)

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraph (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent, or

(f) he did not himself invent the subject matter sought to be patented, or

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. 103. CONDITIONS FOR PATENTABILITY; NON-OBVIOUS SUBJECT MATTER (Applicable Portion)

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

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John B. Lungmus(18,566)	Patrick D. Ertel (26,877)	James J. Napoli (32,361)	James A. Flight (37,622)
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Richard H. Anderson (26,526)			

Send correspondence to: James P. Zeller

FIRM NAME	PHONE NO.	STREET	CITY & STATE	ZIP CODE
Marshall, Gerstein & Borun	312-474-6300	6300 Sears Tower 233 South Wacker Drive	Chicago, Illinois	60606-6402

Full Name of First or Sole Inventor Karl-Christian Gallert	Citizenship Germany
Residence Address - Street Rendeler Strasse 91	Post Office Address - Street Rendeler Strasse 91
City (Zip) D-61184 Karben	City (Zip) D-61184 Karben
State or Country Germany	State or Country Germany
Date ☒	Signature ☒

Full Name of First or Sole Inventor Holger Bengs	Citizenship Germany
Residence Address - Street Bindingstrasse 3	Post Office Address - Street Bindingstrasse 3
City (Zip) D-60598 Frankfurt am Main	City (Zip) D-60598 Frankfurt am Main
State or Country Germany	State or Country Germany
Date ☒	Signature ☒

Second Joint Inventor, if any Claus Simandi	Citizenship Germany
Residence Address - Street Sossenheimer Mühlgasse 10	Post Office Address - Street Sossenheimer Mühlgasse 10
City (Zip) D-65936 Frankfurt an Main	City (Zip) D-65936 Frankfurt an Main
State or Country Germany	State or Country Germany
Date ☒ 24/01/01	Signature ☒ C. Sim